

## REMARKS

The fee for a three-month extension of time, the fee for two additional independent claims and any other fees that may be due in connection with the filing of this paper or with this application should be charged to Deposit Account No. 50-0911. If a Petition for extension of time is needed, this paper is to be considered such Petition.

Claims 1-17, 19-25, 27-35, 62-70, 72-78 and 82-86 are pending. Claims 69, 70 and 72-77 are withdrawn but are retained for possible joinder if claim 1 is deemed allowable.

Claims 5 and 7, which are not included in any rejection and appear to be free of the cited art, are amended to be independent claims by including every limitation of claim 1 from which they originally depended.

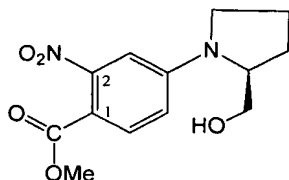
Claims 1, 2, 22, 23, 28-30, 62, 83 and 84 are amended. The claims are amended to comport with the elected subject matter to recite that  $n$  is 0 and  $Z$  is  $CR^A R^B$ . In accord with this amendment, claims 1, 2, 30 and 83 are amended to delete the proviso stating that if  $R^1$  is  $NO_2$  and  $R^3$  is F then  $Z$  is not O, which now is superfluous since  $Z$  is  $CR^A R^B$ . Claims 1, 2 and 30 also are amended to delete " $C_1$ - $C_8$  heteroalkyl" and " $CO_2 R^A$ " as selections in the definition of substituent  $R^9$ . Claims 22, 23, 62 and 84 are amended to comport with the amendment to the definition of substituent  $R^9$ . Claims 1, 2, 30 and 83 are amended to separate the definitions of substituent  $R^A$  and  $R^B$  and to delete  $C_1$ - $C_4$  heteroalkyl as a selection in the definition of  $R^A$ . No new matter is added.

### I. THE PENDING CLAIMS

The Office Action, in the *Office Action Summary* and on page 2, states that claims 1-17, 19-25, 27-35, 62-68, 70, 72-78 and 82-86 are pending in this application. Applicant respectfully submits that this is not accurate. Claim 69 also is pending in this application. Claim 69, directed to non-elected subject matter, is withdrawn for consideration but is retained for possible joinder if claim 1 is deemed allowable.

### II. THE REJECTION OF CLAIMS 1, 8-16, 19-25, 27, 63-68, 78, 82, 83 AND 85 UNDER 35 U.S.C. §102(b) AS ANTICIPATED BY YAMADA *ET AL.*

Claims 1, 8-16, 19-25, 27, 63-68, 78, 82, 83 and 85 are rejected under 35 U.S.C. §102(b) as being anticipated by Yamada *et al.* (WO 2001083460) because Yamada *et al.* discloses the compound RN 372117-90-3 CA PLUS:



The Examiner states this compound of Yamada *et al.* encompassed by the rejected claims when R<sup>1</sup> is COR<sup>A</sup> and R<sup>A</sup> is heteroalkyl because, as defined in the specification, the heteroalkyl purportedly can be O-CH<sub>3</sub>.

### RELEVANT LAW

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. *In re Spada*, 15 USPQ2d 1655 (Fed. Cir., 1990), *In re Bond*, 15 USPQ 1566 (Fed. Cir. 1990), *Soundsciber Corp. v. U.S.*, 360 F.2d 954, 148 USPQ 298, 301, adopted 149 USPQ 640 (Ct. Cl.) 1966. See, also, *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913,1920 (Fed. Cir.), *cert. denied*, 110 S.Ct. 154 (1989).

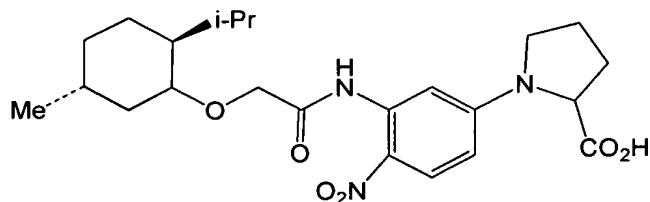
"[A]ll limitations in the claims must be found in the reference, since the claims measure the invention." *In re Lang*, 644 F.2d 856, 862, 209 USPQ 288, 293 (CCPA 1981). It is incumbent on Examiner to identify wherein each and every facet of the claimed invention is disclosed in the reference. *Lindemann Maschinen-fabrik GmbH v. American Hoist and Derrick Co.*, 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984). Further, the reference must describe the invention as claimed sufficiently to have placed a person of ordinary skill in the art in possession of the invention. *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981).

### ANALYSIS

Independent claims 1 and 83 are amended to delete heteroalkyl as a selection in the definition of substituent R<sup>A</sup>, rendering the rejection moot.

### III. THE REJECTION OF CLAIMS 1-4, 8-17, 19-25, 27-35, 62-68, 78 AND 82-86 UNDER 35 U.S.C. §102(b) AS ANTICIPATED BY YE *ET AL.*

Claims 1-4, 8-17, 19-25, 27-35, 62-68, 78 and 82-86 are rejected under 35 U.S.C. § 102(b) as anticipated by Ye *et al.* (Bioorganic & Medicinal Chemistry Letters 13(10): 3361-3365 (2003)) because the reference describes the following compound:



The Examiner states that this compound is encompassed by the rejected claims when R<sup>2</sup> is NHCOR<sup>A</sup> when R<sup>A</sup> is a substituted heteroalkyl.

## ANALYSIS

### Claims 21 and 32

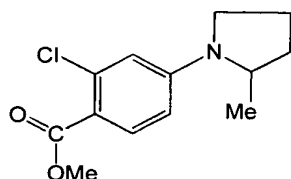
As a preliminary matter, Applicant respectfully submits that Claims 21 and 32 should not have been included in this rejection. The cited compound of Ye *et al.* includes a -COOH substituent on the carbon at position 9 (corresponding to the carbon atom substituted with R<sup>9</sup>). Claim 21 recites that R<sup>9</sup> is selected from among an optionally substituted C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> haloalkyl, CH(R<sup>D</sup>)OR<sup>A</sup>, and CH(R<sup>D</sup>)NR<sup>A</sup>R<sup>B</sup>. Claim 32 recites that R<sup>9</sup> is an optionally substituted C<sub>1</sub>-C<sub>6</sub> heterohaloalkyl. Hence, neither claim 21 nor claim 32 encompasses compounds where R<sup>9</sup> is COOH.

### Independent Claims 1, 30 and 83

As amended, independent claims 1, 30 and 83 do not recite heteroalkyl as a selection for R<sup>A</sup>, thereby rendering this rejection moot.

## IV. THE REJECTION OF CLAIMS 1, 8-17, 19-21, 24, 25, 27, 63-68, 78, 82, 83 AND 85 UNDER 35 U.S.C. §102(b) AS ANTICIPATED BY KOSHIO *ET AL.*

Claims 1, 8-17, 19-21, 24, 25, 27, 63-68, 78, 82, 83 and 85 are rejected under 35 U.S.C. § 102(b) as anticipated by Koshio *et al.* (WO 2003042181) because the reference describes the compound RN 530091-52-2:



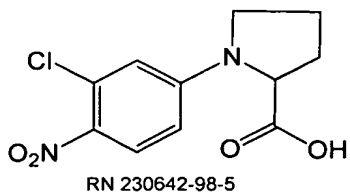
The Examiner states that this compound is encompassed by the rejected claims when R<sup>1</sup> is COR<sup>A</sup> when R<sup>A</sup> is heteroalkyl because, as defined in the specification, the heteroalkyl can be O-CH<sub>3</sub>.

## ANALYSIS

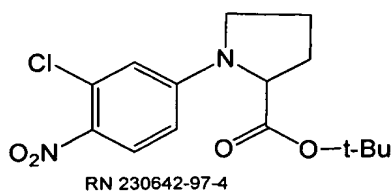
Independent claims 1 and 83 are amended to delete heteroalkyl as a selection in the definition of substituent R<sup>A</sup>, rendering the rejection moot.

## V. THE REJECTION OF CLAIMS 1-4, 6, 8-16, 19, 20, 23-25, 27, 28, 30-35, 63-68, 78, 82, 83 AND 85 UNDER 35 U.S.C. §102(b) AS ANTICIPATED BY AHMAD *ET AL.*

Claims 1-4, 6, 8-16, 19, 20, 23-25, 27, 28, 30-35, 63-68, 78, 82, 83 and 85 are rejected under 35 U.S.C. § 102(b) as anticipated by Ahmad *et al.* (WO 2001027107) because the reference describes the compounds RN 230642-98-5 and RN 230642-97-4:



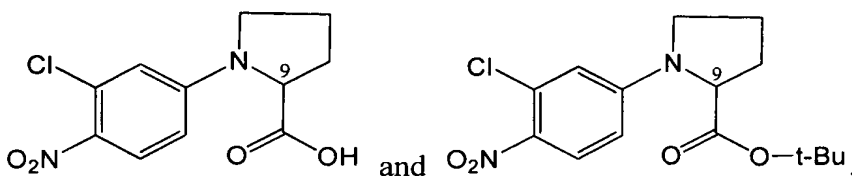
and



The Examiner states these compounds are within the scope of the instant claims when R<sup>1</sup> is NO<sub>2</sub>, R<sup>2</sup> is Cl and the rest of the R groups are hydrogen and/or make pyrrolidine-carboxylic acid/esters.

### DISCLOSURE OF THE CITED ART

Ahmad *et al* discloses heterocyclic sodium/proton exchange inhibitors. Among the compounds described in Ahmad *et al.* are the compounds:



where the carbon atom at position 9 is substituted with either a -COOH or -COO-*t*-Bu moiety.

### ANALYSIS

#### Claim 32

As a preliminary matter, Applicant respectfully submits that claim 32 should not have been included in this rejection. The cited compound of Ahmad *et al.* includes a -COOH substituent on the carbon at the position corresponding to the carbon atom substituted with R<sup>9</sup>. Claim 32 recites that R<sup>9</sup> is an optionally substituted C<sub>1</sub>-C<sub>6</sub> heterohaloalkyl. Thus, claim 32 does not encompass a compound where R<sup>9</sup> is COOH.

#### Independent Claims 1 and 30

The compounds of formula II of instant claims 1 and 30 recite that R<sup>9</sup> is selected from among an optionally substituted C<sub>1</sub>-C<sub>8</sub> alkyl, an optionally substituted C<sub>2</sub>-C<sub>8</sub> alkenyl, an optionally substituted C<sub>1</sub>-C<sub>8</sub> haloalkyl, an optionally substituted C<sub>2</sub>-C<sub>8</sub> haloalkenyl, an optionally substituted C<sub>2</sub>-C<sub>8</sub> heteroalkenyl, an optionally substituted C<sub>2</sub>-C<sub>8</sub> alkynyl, an optionally substituted C<sub>2</sub>-C<sub>8</sub> haloalkynyl, an optionally substituted C<sub>2</sub>-C<sub>8</sub> heteroalkynyl, an optionally substituted heteroaryl, CH(R<sup>D</sup>)OR<sup>A</sup>, CH(R<sup>D</sup>)NR<sup>A</sup>R<sup>B</sup>, COR<sup>A</sup>, and (CH<sub>2</sub>)<sub>m</sub>R<sup>C</sup>. Substituent R<sup>9</sup> in claims 1 and 30 does not include hydrogen as a selection and does not encompass a -COOH or -COO-*t*-Bu moiety.

The compounds of Ahmad *et al.* include a pendent pyrrolidine ring. The one carbon atom adjacent to the ring nitrogen atom contains two hydrogen atoms as substituents, and the other carbon atom adjacent to the ring nitrogen is substituted with a hydrogen atom and a

–COOH or –COO-*t*-Bu moiety. Hence, even though the pendent pyrrolidine can rotate, the carbon atom adjacent to the ring nitrogen atom containing two hydrogen atoms as substituents must correlate to the carbon atom substituted with substituents R<sup>6a</sup> and R<sup>7a</sup> in formula II of the instant claims, since R<sup>9</sup> cannot be hydrogen. Further, since the compounds of Ahmad *et al.* include a hydrogen atom and a –COOH or –COO-*t*-Bu moiety on the carbon atom corresponding to the to the carbon atom substituted with substituents R<sup>9</sup> and R<sup>10</sup> in formula II of the instant claims, R<sup>10</sup> must be hydrogen, requiring that R<sup>9</sup> encompass the –COOH and –COO-*t*-Bu moieties of Ahmad *et al.* In the instant claims, substituent R<sup>9</sup> does not encompass –COOH and –COO-*t*-Bu. Thus, the compounds of Ahmad *et al.* are not encompassed by independent claims 1 and 30.

Ahmad *et al.* does not describe any compound substituted at position 9 with a moiety selected from among an optionally substituted C<sub>1</sub>-C<sub>8</sub> alkyl, an optionally substituted C<sub>2</sub>-C<sub>8</sub> alkenyl, an optionally substituted C<sub>1</sub>-C<sub>8</sub> haloalkyl, an optionally substituted C<sub>2</sub>-C<sub>8</sub> haloalkenyl, an optionally substituted C<sub>2</sub>-C<sub>8</sub> heteroalkenyl, an optionally substituted C<sub>2</sub>-C<sub>8</sub> alkynyl, an optionally substituted C<sub>2</sub>-C<sub>8</sub> haloalkynyl, an optionally substituted C<sub>2</sub>-C<sub>8</sub> heteroalkynyl, an optionally substituted heteroaryl, CH(R<sup>D</sup>)OR<sup>A</sup>, CH(R<sup>D</sup>)NR<sup>A</sup>R<sup>B</sup>, COR<sup>A</sup> and (CH<sub>2</sub>)<sub>m</sub>R<sup>C</sup>. Thus, none of the compounds described in Ahmad *et al.* includes every element of claims 1 and 30. Claims 2-4, 6, 8-16, 19, 20, 23-25, 27, 28, 63-68, 78 and 82 ultimately depend from claim 1. Claims 31-35 ultimately depend from claim 30. Therefore, Ahmad *et al.* does not anticipate any of claims 1-4, 6, 8-16, 19, 20, 23-25, 27, 28, 30-35, 63-68, 78 and 82.

#### Independent Claim 83

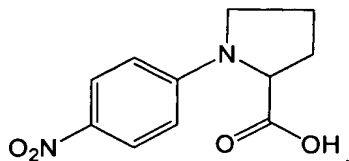
The compounds of formula II of instant claim 83 recite that R<sup>9</sup> is selected from among CH(R<sup>D</sup>)OR<sup>A</sup>, CH(R<sup>D</sup>)NR<sup>A</sup>R<sup>B</sup> and COR<sup>A</sup>. Substituent R<sup>9</sup> in claim 83 does not include hydrogen as a selection and does not encompass a –COOH or –COO-*t*-Bu moiety.

As discussed above, because of the presence of hydrogen substituents on the carbon atoms adjacent to the ring nitrogen atom of the pendent ring, the carbon atom adjacent to the ring nitrogen atom containing two hydrogen atoms as substituents must correlate to the carbon atom substituted with substituents R<sup>6a</sup> and R<sup>7a</sup> in formula II of the instant claims, and the other carbon atom substituted with a hydrogen requires that R<sup>10</sup> must be hydrogen, and thus R<sup>9</sup> would need to encompass –COOH and –COO-*t*-Bu in order for the compounds of Ahmad *et al.* to be encompassed by instant claim 83. In instant claim 83, substituent R<sup>9</sup> does not encompass –COOH and –COO-*t*-Bu. Thus, the compounds of Ahmad *et al.* are not encompassed by independent claim 83, nor any pending claim.

Ahmad *et al.* does not describe any compound substituted at position 9 with a moiety selected from among  $\text{CH}(\text{R}^{\text{D}})\text{OR}^{\text{A}}$ ,  $\text{CH}(\text{R}^{\text{D}})\text{NR}^{\text{A}}\text{R}^{\text{B}}$  and  $\text{COR}^{\text{A}}$ . Thus, none of the compounds described in Ahmad *et al.* includes every element of claim 83. Claims 84 and 85 ultimately depend from claim 83. Therefore, Ahmad *et al.* does not anticipate any of claims 83-85.

**V. THE REJECTION OF CLAIMS 83-85 UNDER 35 U.S.C. §102(b) AS ANTICIPATED BY YOSHINO *ET AL.***

Claims 83-85 are rejected under 35 U.S.C. 102(b) as being anticipated by Yoshino *et al.* (Technology Reports of the Osaka University 40(1986-2003), pages 81-85), which describes the compound RN 129297-51-4, having the structure:



**ANALYSIS**

The cited compound of Yoshino *et al.* is not within the scope of independent claim 83 nor any pending claim. The compounds of formula II of instant claim 83 recite that  $\text{R}^9$  is selected from among  $\text{CH}(\text{R}^{\text{D}})\text{OR}^{\text{A}}$ ,  $\text{CH}(\text{R}^{\text{D}})\text{NR}^{\text{A}}\text{R}^{\text{B}}$  and  $\text{COR}^{\text{A}}$ . As discussed above, because of the presence of hydrogen substituents on the carbon atoms adjacent to the ring nitrogen atom of the pendent ring, the carbon atom adjacent to the ring nitrogen atom containing two hydrogen atoms as substituents must correlate to the carbon atom substituted with substituents  $\text{R}^{6\text{a}}$  and  $\text{R}^{7\text{a}}$  in formula II of the instant claims, the other carbon atom substituted with a hydrogen requires that  $\text{R}^{10}$  is hydrogen, and thus  $\text{R}^9$  would need to encompass  $\text{COOH}$ .  $\text{R}^9$  in claim 83 does not encompass  $-\text{COOH}$ . Thus, the compounds of Yoshino *et al.* are not encompassed by independent claim 83.

Yoshino *et al.* does not describe any compound substituted at position 9 with a moiety selected from among  $\text{CH}(\text{R}^{\text{D}})\text{OR}^{\text{A}}$ ,  $\text{CH}(\text{R}^{\text{D}})\text{NR}^{\text{A}}\text{R}^{\text{B}}$  and  $\text{COR}^{\text{A}}$ . Thus, none of the compounds described in Yoshino *et al.* includes every element of claim 83. Claims 84 and 85 ultimately depend from claim 83. Therefore, Yoshino *et al.* does not anticipate any of claims 83-85.

**VI. THE REJECTION OF CLAIMS UNDER 35 U.S.C. §112, 2<sup>ND</sup> PARAGRAPH**

Claim 62 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter because the first recited compound of claim 62 lacks antecedent basis.

Without acquiescing to or addressing the propriety of the rejection, in order to advance prosecution, claim 62 is amended to delete the first recited compound. Thus, the amendment obviates the rejection.

## **VII. CLAIM OBJECTION**

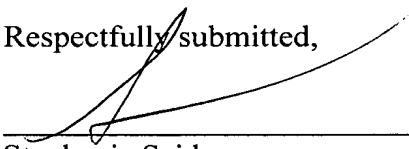
The Office Action states that the scope of formula (II) of independent claims 1 and 83 is drawn to different Markush structures.

As pending, claim 83 is a subgenus of the originally claimed genus of compounds of Formula II. When compared to Claim 1, Claim 83 includes additional alternative substituents in the definition of  $R^2$  and states that  $R^{6a}$  and  $R^{7a}$  taken together can form a carbonyl. These features were deleted from original claim 1. The scope of claim 83 is encompassed by original claim 1 and accordingly previously was searched. Since claim 83 reads on the elected group and includes searched subject matter, Applicant respectfully submits that it is not improper to include independent claim 83 in this application.

\* \* \*

In view of the amendment and remarks herein, entry of the amendment, reconsideration and allowance of the application respectfully are requested.

Respectfully submitted,



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